

IN THE CLAIMS

Please amend the claims as follows:

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a
6/29/06

Claim 1. (Currently Amended) ~~A crystal of a hydrochloride of~~ Crystalline N-{2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(5-methyl-3-isoxazolyl)urea monohydrochloric acid salt monohydrate, ~~wherein said hydrochloride is a hydrochloric acid monoadduct and a monohydrate.~~

Claims 2-12. (Cancelled)

²
Claim ~~13~~. (Currently Amended) The ~~crystal~~ crystalline compound according to claim 1, wherein in powder X-ray diffractometry, the ~~crystal~~ crystalline compound has peaks with not less than 10% relative intensity at at least the following diffraction angles (2θ):

Table A-1

Diffraction angle (2θ)

11.47 ± X

22.59 ± X

23.02 ± X

26.27 ± X

26.63 ± X

wherein X is 0 to 0.20.

³
Claim ~~14~~. (Currently Amended) The ~~crystal~~ crystalline compound according to claim 13, wherein the relative intensity in said diffraction angles (2θ) is not less than 15%.

⁴
Claim ~~15~~. (Currently Amended) The ~~crystal~~ crystalline compound according to claim 13, wherein the relative intensity in said diffraction angles (2θ) is not less than 20%.

⁵
Claim ~~16~~. (Currently Amended) The ~~crystal~~ crystalline compound according to claim 13, wherein the relative intensity in said diffraction angles (2θ) is not less than 25%.

⁶
Claim ~~17~~. (Currently Amended) The ~~crystal~~ crystalline compound according to claim 13, wherein the relative intensity in said diffraction angles (2θ) is not less than 30%.

Claim ⁷~~18~~. (Currently Amended) The ~~crystal~~ crystalline compound according to any one of claims 13 to 17, wherein X is 0 to 0.10.

Claim ⁸~~19~~. (Currently Amended) The ~~crystal~~ crystalline compound according to claim 1, wherein in powder X-ray diffractometry, the ~~crystal~~ crystalline compound has peaks with not less than 10% relative intensity at at least the following diffraction angles (2 θ):

Table B-1

Diffraction angle (2 θ)

8.76 \pm X

11.47 \pm X

15.28 \pm X

17.16 \pm X

17.53 \pm X

18.80 \pm X

20.02 \pm X

22.59 \pm X

23.02 \pm X

25.32 \pm X

25.43 \pm X

26.27 \pm X

26.63 \pm X

27.00 \pm X

28.57 \pm X

wherein X is 0 to 0.20.

Claim ⁹~~20~~. (Currently Amended) The ~~crystal~~ crystalline compound according to claim 19, wherein the relative intensity in said diffraction angles (2 θ) is not less than 15%.

Claim ¹⁰~~21~~. (Currently Amended) The ~~crystal~~ crystalline compound according to claim 19, wherein the relative intensity in said diffraction angles (2 θ) is not less than 20%.

¹¹
Claim ~~22~~. (Currently Amended) The ~~crystal~~ crystalline compound according to any one of claims 19 to 21, wherein X is 0 to 0.10:

¹²
Claim ~~23~~. (Currently Amended) The ~~crystal~~ crystalline compound according to claim 1, wherein in powder X-ray diffractometry, the ~~crystal~~ crystalline compound has the following diffraction angles (2 θ) and relative intensities:

Table 1

Diffraction angle (2 θ)	Relative intensity
8.76	22
11.47	100
15.28	21
17.16	21
17.53	23
18.80	21
20.02	25
22.59	35
23.02	37
25.32	29
25.43	23
26.27	36
26.63	32
27.00	29
28.57	28

Claims 24-50 (Cancelled).

Sub
Ex.
Amend
Claim 51. (Currently Amended) A process for producing a ~~crystal of hydrochloride~~ of crystalline N-{2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(5-methyl-3-isoxazolyl)urea monohydrochloric acid salt monohydrate, ~~wherein said hydrochloride is a hydrochloric acid monoadduct and a monohydrate~~, said process comprising the steps of:
adding hydrochloric acid and ethanol to a solution of N-{2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(5-methyl-3-isoxazolyl)urea in an aprotic polar solvent; and precipitating crystals from the solution.

2.

Examiner's amendment

Authorization for this examiner's amendment was given in a telephone interview with J. Derek Mason on Jun. 29, 2006.

Claim ~~51~~¹³ (currently amended)

A process for producing crystalline N-{2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(5-methyl-3-isoxazolyl)urea monhydrochloric acid salt monohydrate, said process comprising the steps of:

adding hydrochloric acid to a solution of N-{2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(5-methyl-3-isoxazolyl)urea in an aprotic polar solvent selected from N,N-dimethylformamide and N,N-dimethylacetamide;

adding ethanol and water to the above solution to precipitate crystals from the solution.

Claims 52 and 53, 74-78 are canceled.

3.

Reason for Allowance

The following is an examiner's statement of reasons for allowance:

Applicants have limited the claims to one compound which was disclosed on pages 7-8 of the specification. This compound has been properly provided with its nomenclature by CAS (see CA140:363009, RN 682745-41-1) and the name has been properly incorporated as claim 1. Such product has an advantage over the known compound in that it was found that hygroscopicity for the claimed compound to be on a low level, thus, is expected to have the advantage to be stable under high humidity conditions (see p.76 and p. 2 of the specification). The closest prior art was found in US 6,821,987 wherein a hydrochloric acid salt was prepared. The reference disclose generically possible formation of solvate. However, no solvate in any form or with any solvent or water was described and the formation of the hydrochloric acid addition salt of the instantly claimed compound was crystallized from non-aqueous solutions, thus, free from any hydrate (see col. 22, example 21, lines 53-63). Claims 1, 13-23, 51, 54-55, 79 are allowed.

Claim 52. (Original) The process according to claim 51, wherein, in addition to hydrochloric acid and ethanol, water is further added.

Claim 53. (Previously Presented) The process according to claim 51, wherein said aprotic polar solvent is N,N-dimethylformamide or N,N-dimethylacetamide.

¹⁴
Claim ~~54~~. (Previously Presented) The process according to claim 51, wherein said hydrochloric acid has a concentration of 10 to 14 N.

¹⁵
Claim ~~55~~. (Previously Presented) The process according to claim 51, wherein in powder X-ray diffractometry, the crystal has peaks with not less than 10% relative intensity at at least the following diffraction angles (2 θ):

Table A-1

Diffraction angle (2 θ)

11.47 \pm X

22.59 \pm X

23.02 \pm X

26.27 \pm X

26.63 \pm X

wherein X is 0 to 0.20.

Claims 56-73 (Cancelled)

Claim 74. (Previously Presented) The process according to claim 52, wherein said aprotic polar solvent is N,N-dimethylformamide or N,N-dimethylacetamide.

Claim 75. (Previously Presented) The process according to claim 52, wherein said hydrochloric acid has a concentration of 10 to 14 N.

Claim 76. (Previously Presented) The process according to claim 53, wherein said hydrochloric acid has a concentration of 10 to 14 N.

Claim 77. (Previously Presented) The process according to claim 52, wherein in powder X-ray diffractometry, the crystal has peaks with not less than 10% relative intensity at at least the following diffraction angles (2θ):

Table A-1

Diffraction angle (2θ)

11.47 \pm X

22.59 \pm X

23.02 \pm X

26.27 \pm X

26.63 \pm X

wherein X is 0 to 0.20.

Claim 78. (Previously Presented) The process according to claim 53, wherein in powder X-ray diffractometry, the crystal has peaks with not less than 10% relative intensity at at least the following diffraction angles (2θ):

Table A-1

Diffraction angle (2θ)

11.47 \pm X

22.59 \pm X

23.02 \pm X

26.27 \pm X

26.63 \pm X

wherein X is 0 to 0.20.

¹⁶
Claim 79. (Previously Presented) The process according to claim 54, wherein in powder X-ray diffractometry, the crystal has peaks with not less than 10% relative intensity at at least the following diffraction angles (2θ):

Table A-1

Diffraction angle (2θ)

11.47 \pm X

22.59 \pm X

23.02 \pm X

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$26.27 \pm X$

$26.63 \pm X$

wherein X is 0 to 0.20.